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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,453	09/13/2000	Steven M. Ruben	PZ038P1	8927

22195 7590 03/23/2004

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EXAMINER	
MARSCHEL, ARDIN H	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/661,453	RUBEN ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2003 and 09 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-36,39-43,46-50,53-57 and 60-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24,28-30,34 and 35* is/are allowed.

6)☒ Claim(s) *25-27,31-33,36,39-43,46-50,53-57, and 60-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 9/26/03 and 1/9/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NEW MATTER

Claims 25, 31, 36, 39-43, 46-50, 53-57, and 60-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is reiterated and maintained from the previous office action, mailed 6/26/03. Applicants arguments, filed 9/26/03, are reiterations of previously filed arguments which were already indicated as non-persuasive in the previous office action, mailed 6/26/03. In summary, applicants argue firstly that reading the entire specification and reviewing claim 25 and 31 would easily and reasonably result in concluding that applicants had possession of SEQ ID NO: 73 without its initial Methionine. As has been responded to before there is no written disclosure as filed which reasonably leads to that conclusion. There is no sequence disclosed as filed which is the same as SEQ ID NO: 73 minus its intial Methionine. The closest set of descriptions as filed is that of

SEQ ID NO: 73 itself "with" its initial Methionine and then the descriptions on page 150, line 31, and page 151, lines 1-6, that polypeptides of the invention "may" include an initial Methionine and that it is well known in the art that the N-terminal methionine "generally" is removed with "high efficiency" from any protein after translation in all eukaryotic cells. The word "may" as well as the "high efficiency" general removal of said initial Methionine lacks inherent reasonable disclosure for SEQ ID NO: 73 having its initial Methionine removed. It is acknowledged that "maybe" this occurs for SEQ ID NO: 73, but written basis for specific possession of the specific invention of SEQ ID NO: 73 without its initial Methionine is lacking in this combination of disclosures. Written basis for an invention is not supported by what may or may not be obvious. Applicants seem to be indicating that it is obvious that since a common or general high efficiency removal of an initial Methionine from a translated protein in eukaryotes, that it therefore must inherently occur for SEQ ID NO: 73 to result in the claimed invention of instant claims 25 and 31. Applicants are reminded that what is inherent and therefore has written support via such inherency is different from what may or may not be obvious. Applicants are also reminded that "high efficiency" is different from total or 100% efficiency. A total or 100% efficiency has not been disclosed as filed for the removal of an initial Methionine from SEQ ID NO: 73. Applicants then argue that written basis is supported by what could reasonably be concluded. In response a "high efficiency" of removal of initial Methionine without specifying that this has occurred for SEQ ID NO: 73 per se that applicants had possession of such a initial Methionine removed SEQ ID NO: 73 is not deemed to be a reasonable conclusion due to a lack of specific disclosure of

such a Methionine removal for SEQ ID NO: 73 per se as is instantly claimed. Applicants then argue that a literal description of an invention is not required citing the MPEP at 2163.02. In response this MPEP section supports the written description and possession of the invention when words that reasonably support the invention are utilized that differ from the claimed wording but have the same disclosure of subject matter. Thus, the meaning must be present to provide written basis for an invention but is inclusive of alternate wording which still describes the same invention. In response to this argument the meaning of the possession of a Methionine removed SEQ ID NO: 73 is still deemed to be lacking in the instant disclosure as filed. At best the suggestion that the removal of such a Methionine may occur and generally does with high efficiency lacks specific disclosure in meaning or possession of the invention where such a Methionine is actually lacking from SEQ ID NO: 73 as now claimed. This argument therefore is moot regarding this rejection because the meaning of a specific Methionine removed SEQ ID NO: 73 is not anywhere disclosed in the instant disclosure as filed. Applicants then review their arguments however do not set forth any new arguments on the last section regarding this rejection on page 11 of their REMARKS, filed 9/26/03.

NEW MATTER has additionally been added to claims 36, 43, 50, 57, 64, and 69 regarding the functional limitation therein added directed to polypeptides expressed in adrenal gland tumors other than SEQ ID NO: 73. These claims are inclusive of non-identical polypeptides to the extent of being as different such that only 90% identity remains to SEQ ID NO: 73 or fragments thereof such as a 82 amino acid fragment as in instant claim 36, or, alternatively, as fragment of only 30 contiguous amino acid

residues as in claims 64 or 69. It is acknowledged that applicants pointed to page 58, lines 16-18, for written support in their REMARKS, filed 9/26/03. Consideration of said page 58 support only supports the concept that the gene product of gene 23, apparently which is described as SEQ ID NO: 73 is actually expressed in adrenal gland tumors, not fragments as small as 30 amino acid residues or nonidentical polypeptides with 90% or more identity to SEQ ID NO: 73 or certain fragments thereof as instantly claimed. This inclusion of said functional limitation in claims 36 etc. now sets forth this expression in adrenal gland tumors for all of these nonidentical polypeptides and fragments as discussed above which is not supported as filed and therefore is NEW MATTER. Claims which depend from claims 36, 43, 50, 57, 64, and 69 directly or indirectly are also included as rejected hereinunder due to their dependence. This rejection is necessitated by amendment.

LACK OF SCOPE OF ENABLEMENT

Claims 25-27, 31-33, 36, 39-43, 46-50, 53-57, and 60-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting only of the entirety of SEQ ID NO: 73, does not reasonably provide enablement for fragments of SEQ ID NO: 73. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at

1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

This rejection is reiterated and maintained from the previous office action, mailed 6/26/03. Applicants firstly argue that amendments to claims 24 etc. have added a functional limitation to these pending claims. Consideration of the amending of the instant claim set reveals that confusingly no such functional limitation has been added to claims 24 or 30, however, added to other claims in the list. Applicants argue that evaluation of enablement is not to be directed to enabling any or all alterations that can be made in the claimed proteins but rather whether proteins as claimed have a single use and that this use can be confirmed, without undue experimentation. This is acknowledged. Applicants then argue at length about the possibility of utilizing the polypeptide fragments for various uses such as receptor binding, antibody generation etc. These are allegations of possible uses but do not eliminate, or even estimate the amount of, the massive testing requirements to hunt for those fragments which have such activities. Applicants then point to the specification on pages 75 and 90-97 of the

specification for procedures for such hunting. Consideration of said pages reveals that page 75 suggests that screening may be applied to find variants without any suggestion as to what screening method is to be utilized. On pages 90-97 the majority of this citation is directed to sequence matching methods which are well known but moot regarding this rejection because sequence matching only speculatively leads to function determinations. On pages 95-96 some protein examples are set forth that can be altered severely without losing function as well as conservative amino acid substitution options. In response this does not support the alteration or fragmentation functionality of SEQ ID NO: 73 because there is no description of how sensitive SEQ ID NO: 73 is to alteration in sequence or fragmentation with still retaining activity or function. It is just as well known that certain proteins severely lose activity when only a single amino acid change occurs, such as the disease state which is precipitated by a single amino acid change in Sickle Cell Anemia. Whether SEQ ID NO: 73 is insensitive to alternation or fragmentation has not been disclosed as filed nor is readily determined without a significant research project directed to a multitude of segments of said SEQ ID NO: 73, none of which have been instantly described to even start such a massive research project. In summary this rejection is still deemed proper for the reasons set forth above and of record.

Claims 24, 28-30, 34, and 35 are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

March 19, 2004

Ardin H. Marschel 3/19/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER